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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/528,742	03/20/2000	Paul Roben	11390-002001	5781

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/528,742	ROBEN ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13,14,16-34,36-46,49,51 and 55-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,14,16-34,36-46,49,51 and 55-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *March 20, 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 26, 2003, paper number 23, has been entered.

DETAILED ACTION

This application filed March 20, 2000, claims benefit to provisional application 60/139,579, filed June 17, 1999.

Applicant's amendment, filed August 26, 2003, paper number 23, has been received and entered. Claims 11, 12, 15, 35, 47, 48, 50, 52-54 have been canceled. Claims 1, 10, 30, 31, 46, 49, 51 and 55 have been amended. Claims 56-61 have been added. Claims 1-10, 13, 14, 16-34, 36-46, 49, 51 and 55-61 are pending.

Election/Restriction

Upon review of the teachings of the specification and the nature of the claimed invention, and in view of discussions with Applicant's (informal phone interview) the election of

species of a specific (a) labeling domain and (b) specific binding domain is withdrawn. Specifically, upon reconsideration of the claimed invention, Examiner notes that the inventive concept focuses on the observation that after labeling cells present in the lumenal space by methods known in the art, specific washing conditions provide a means to reduce non-specific binding and allow for the identification lumen exposed molecules. This appears to be due in part to the species of cleavable moiety that is not cleavable under *in vivo* conditions but is cleavable under conditions that does not denature the lumen-expose molecule (as reflected in newly amended claims). Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claims 1-10, 13, 14, 16-34, 36-46, 49, 51 and 55-61 are currently under examination as they are drawn to the elected species of the cleavable moiety dithiopropionate.

Claim Objections

Claim 57 is objected to because of the following informalities: it is dependent on canceled claim 11. For the sake of compact prosecution it is being interpreted to be drawn to claim 10 and encompass generally types of labeling molecules.

Appropriate correction is required.

Claims 1, 19, 30, 51 stand objected to because the claims recite and encompass species which were not specifically elected.

As discussed above, Examiner has withdrawn the restriction requirement for the species of the first and second domains of the binding reagent, however the restriction requirement of the species of the cleavable domain is maintained. It is noted that upon finding a generic claim allowable, Applicants are entitled to consideration of claims to additional species however as set forth below, the claims as they are drawn to the elected species are not found allowable. Therefore, because the elected species and a generic claim has not been found allowable, the objection is maintained.

Specification

The objection to the amendment filed September 10, 2002, paper number 16, is maintained. The specification is objected to under 35 U.S.C. 132 because the amendment introduced new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. As indicated in the previous office action, the added material which is not supported by the original disclosure is as follows: the amendment to the specification in the claim for priority includes the phrase "the disclosure of which is incorporated herein by reference in its entirety", because this was not recited or part of the original disclosure. It is noted that the after final amendment filed June 2, 2003, paper number 18, had amendments to the specification to delete the phrase, however as indicated in the

advisory action mailed June 13, 2003, paper number 22, the amendment would not be entered. Therefore, the specification has not been amended and still recites the phrase "the disclosure of which is incorporated herein by reference in its entirety".

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Previously pending claims 52-54 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

Cancellation of the claims has rendered the basis of the rejection moot, therefore the rejection is withdrawn.

Claims 1-10, 13, 14, 16-34, 36-46, 49, 51 and 56-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, the claims have been amended to indicate the third domain of the reagent 'is not cleavable under *in vivo* conditions but is cleavable under a condition that does not denature the lumen-exposed molecule' (see for example claim 1). The specification reduces to practice the claimed invention with the compound sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate, however there is no specific teaching for other compounds with these specific properties recited in the claims, nor is there general teaching or evidence of how or what feature of sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate is representative of the genus of the elected species of other cleavable moieties. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells*

Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). Only the compound sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate is reduced to practice in the instant specification, however it is unclear even from this example if the specific conditions do or do not denature lumen exposed molecules. Moreover, there is not even general guidance on any conditions for practicing the claimed methods or conditions for different types of molecules that could be present on the luminal surface of a cell. Again as noted above, there is no specific teaching of other compounds with these specific properties recited in the claims, nor is there general teaching or evidence of how or what feature of sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate is representative of the genus of the elected species of other cleavable moieties. Thus, the specification fails to describe the relevant identifying characteristics of such molecules needed to practice the claimed method. The skilled artisan cannot envision the specific structural features that provide the functional characteristics set forth in the claims, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated:
In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is

normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers,* 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.").

Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence Because Applicants have failed to provide an adequate written description of the materials used in the compositions and methods claimed and because there is no evidence that Applicants possessed such compounds beyond sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate or as more generally set forth in the specification those disclosed and/or known in the prior art, the rejected claims fail to meet the written description requirement under 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 13, 14, 16-34, 36-46, 49, 51 and 55-61 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the claims recite and encompass conditions wherein the 'lumen-exposed molecule' is not denatured, however it is unclear what the metes and bounds of this condition would be. Moreover, the term denaturing is generally reserved and used to describe proteins and it is unclear what it encompasses relative to other molecules identifiable on the cell. For example, if a particular type of lipid is bound and identified what would the denatured state of a lipid be? Moreover, the conditions encompassed by the claim would vary among different proteins because each protein has specific properties inherent to itself. Thus, the metes and bounds of the claims are indefinite because the claimed methods would be subject to conditions that could not be determined *a priori* and are subjective in nature depending on how one determines if a protein or a molecule is denatured.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 52 and 53 rejected under 35 U.S.C. 102(b) as being anticipated by Pierce Catalog & Handbook, 1994-95.

Cancellation of the claims has rendered the basis of the rejection moot, therefore the rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-34, 36-45, 49, 51, 57, 58, 60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over De La Fuente *et al.* (IDS reference), Hastie *et al.* (IDS ref)., and Rothschild *et al.* (US Patent 5,948,624) and the Pierce Catalog & Handbook, 1994-95.

Applicants note the amendments to the claims and summarizing each of the teachings of De La Fuente *et al.*, Hastie *et al.*, and Rothschild *et al.* argue that none references and the compounds taught in Pierce make obvious the method or use of a composition with a third domain encompassed by the instantly claimed invention. Finally, Applicants argue that none of the references teach labeling luminal molecules *in situ* or *in vivo* by administering sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate as set forth in claim 55. See Applicants' amendment, Section IV, pages 10-12. Applicants arguments have been fully considered and found persuasive in part.

With respect to the teaching of the specific compound of sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate, it is noted that this compound was known and commercially available at the time of filing as evidenced by the Pierce catalog (see second compound on the third page of referenced copy of the catalog). Further, as evidenced by the Pierce catalog and the cited references such compounds were used for the labeling and isolation of biological molecules. Therefore, this limitation of claim 55 is provided in the cited references. Further, it is noted that DeLa Fuente *et al.* and Hastie *et al.* provide labeling and isolation conditions that would not denature the protein on the cell *in situ* or the homogenate isolates (see methods section). However, none of the cited references teach to cleave the molecule under conditions that does not denature the labeled protein. Therefore, claims 1-10, 13, 14, 16-18, 46, 55, 56, 59 and 60 would not be obvious over the cited references and the rejection is withdrawn over these claims because of this limitation.

However, with respect to the remaining pending claims it is noted that they do not recite such a limitation and thus do not require any particular condition or cleavage. As set forth in the previous rejection, at the time of filing the compound sold by Pierce was disclosed as useful for labeling molecules on the surface of a cell. Moreover, as noted above the specific compound of sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate, was known and commercially available at the time of filing as evidenced by the Pierce catalog for use as a labeling molecule (see second compound on the third page of referenced copy of the catalog). Because this compound is specifically set forth in claim 55, it is being interpreted to be and to represent a specific structure that provides the characteristics set forth in the claim relative to its cleavability.

Pierce specifically teaches sulfoscccinimidy-2(biotinamidoethyl-1,3-dithioproprionate, and provides detailed guidance of its structure and properties in handling, and more generally of the use of such compounds in the identification and isolation of biological molecules. Each De La Fuente *et al.* and Hastie *et al.* teach to use a similar labeling compound, NHS-LC-biotin, for the identification and isolation of the particular components from the perfusiable space within an organ and on a tissue. Rothschild *et al.* was cited for a general description of heterobifunctional crosslinkers and for their use for the detection and isolation of biomolecules to identify and detect specific conjugates associated with a tissue that can be further used in determining the role of the molecule in the detection of disease or disorders. Clearly, at the time of filing, the labeling of tissues was being practiced and the use of heterobifunctional cross-linkers in these methods was known and practiced. Further, De La Fuente *et al.* clearly states that the methodology can be

used to identify molecules on the luminal surface of a cell (see summary in abstract). Applicants' argument that administering the reagent to an intact organ is unobvious is unpersuasive because De La Fuente *et al.* clearly indicates that the methods are for identifying proteins accessible *via* the circulation. The teachings of De La Fuente *et al.*, Hastie *et al.*, and Rothschild *et al.* taken as a whole clearly teach the use of heterobifunctional cross-linker for labeling molecules on the cell surface of a cell, and that these methods were successfully practiced previously with other cross-linking reagents.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the specific methods of De La Fuente *et al.* and Hastie *et al.* and those more general disclosed by Rothschild *et al.* with the cleavable cross-linkers for sale and discussed in the Pierce Catalog & Handbook.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732. After January 12, 2004, the Examiner's telephone number will be (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. After January 12, 2004, Deborah Reynolds telephone number will be (571)272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141. After January 14, 2004, Dianiece Jacobs telephone number will be (571)272-0532.

Joseph T. Woitach

Joe Woitach

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